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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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DAVID JAFFER PILLSBURY WINTHROP LLP 2475 HANOVER STREET PALO ALTO, CA 94304-1114			EXAMINER BEISNER, WILLIAM H	
			ART UNIT	PAPER NUMBER
			1744	

DATE MAILED: 04/01/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/080,901

Applicant(s)

BONDE ET AL.

Examiner

William H. Beisner

Art Unit

1744

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on ____.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-53 is/are pending in the application.
- 4a) Of the above claim(s) ____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) ____ is/are allowed.
- 6) ☒ Claim(s) 1-53 is/are rejected.
- 7) ☐ Claim(s) ____ is/are objected to.
- 8) ☐ Claim(s) ____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 21 February 2002 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. ____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- ☒ Notice of References Cited (PTO-892)
- ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date ____.
- ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. ____.
- ☐ Notice of Informal Patent Application (PTO-152)
- ☐ Other: ____.

DETAILED ACTION

Information Disclosure Statement

1. The information disclosure statement filed 02 April 2002 has been considered and made of record.

Claim Rejections - 35 USC § 102

2. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

3. Claims 1-4, 6, 7, 9, 10, 21-23, 29 and 30 are rejected under 35 U.S.C. 102(b) as being anticipated by Matson et al.(US 5,429,807).

The reference of Matson et al. discloses a device for exposing a substrate surface to one or more fluids wherein the device includes a substrate (56) including a contiguous target region; a cover plate (12); a plurality of fluid-transporting features (14) present in the cover plate surface; a plurality of inlets (22); at least one outlet (23); and positioning means (70,80,65) for positioning the cover plate surface in fluid-tight contact with the substrate surface such that the partition walls of the cover plate contacts a location on the contiguous target region (See Figures 1-3 and 6).

With respect to claim 2, the substrate can be removed from the cover plate.

Art Unit: 1744

With respect to claim 3, the substrate surface is substantially planar (See column 4, lines 60-65).

With respect to claims 4, 6, 7 and 9, the cover member includes channels (14) that are the same size and substantially parallel to each other and the flow is in the same direction in each channel.

With respect to claim 10, the channels (14) are about 500 micrometers wide (See column 3, lines 45-47).

With respect to claims 21-23, each inlet is capable of being communicated to the same source of fluid or a different source of fluid (See Figures 4 and 5).

With respect to claims 29 and 30, the positioning means allows for the repositioning of the at least one partitioning wall to contact the contiguous target region at a different location by rotational reorientation of the cover plate (See column 6, lines 31).

4. Claims 31-37, 39-46 and 48-53 are rejected under 35 U.S.C. 102(b) as being anticipated by Takayama et al.(Proc. Natl. Acad. Sci.).

With respect to claim 31, the reference of Takayama et al. discloses a method of exposing a substrate surface to a plurality of cells. The method includes providing a substrate having a surface containing a contiguous target region and maintaining a plurality of fluids each in contiguous laminar flow over the target region, wherein each fluid conveys a cell over a distinct exposure zone on the target region, thereby exposing the distinct exposure zone to the cell (See Figures 1 and 2). Note plural lanes of laminar flow exist in a single channel which meet the language of claim 31.

Art Unit: 1744

With respect to claim 32, the PDMS membrane includes “at least one partitioning wall contacting the contiguous target region”.

With respect to claims 33-36, the exposure zones are elongated, substantially parallel, include the same direction of flow, and the same size (See Figure 1).

With respect to claim 37, each fluid conveys a plurality of cells (See Figure 2A).

With respect to claims 39-46, cells are immobilized on the substrate prior to an additional step of flow with respect to the immobilized cells (See Figure 2D and related text).

With respect to claim 48, the reference discloses a method for exposing a substrate surface (Petri dish) to a plurality of fluids that includes providing a substrate (Petri dish) having a surface containing a contiguous target region, a cover plate (PDMS), a plurality of fluid-transporting features (lanes 1, 2 and 3, in Figure 1B), a plurality of inlets (1, 2 and 3, in Figure 1B), at least one outlet (outlet show in Figures 1A and 1B); the cover plate (PDMS) is positioned in fluid-tight contact with the substrate surface (See Figure 1A) such that the three distinct target zones are formed between the inlets and the outlet; and maintaining one or more fluids (see page 5546) in laminar flow through the inlets over the target region.

With respect to claim 49, additional fluid is flowed over the target region in subsequent steps (See the text related to Figures 1C and 1D).

With respect to claims 50-53, the cover (PDMS) can be rotated 90° repositioned on the substrate (See Figure 2D and related text).

Claim Rejections - 35 USC § 103

Art Unit: 1744

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all

obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

6. The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35

U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

7. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

8. Claims 5, 8 and 11 are rejected under 35 U.S.C. 103(a) as being unpatentable over Matson et al.(US 5,429,807).

The reference of Matson et al. has been discussed above.

Art Unit: 1744

With respect to claim 5, while the reference does not specifically disclose the number of channels, the reference does suggest the use of multiple channels. As a result, in the absence of a showing of criticality and/or unexpected results, it would have been obvious to one of ordinary skill in the art to determine the optimum number of channels to employ based merely on considerations such as the size of the channels, the size of the substrate employed and/or the number of contact zones required while maintaining the efficiency of the fluid contacting system.

With respect to claim 8, the reference of Matson et al. discloses that outlets (23) are manifolded to a single waste zone (54) (See Figure 5). As a result, it would have been obvious to one of ordinary skill in the art to provide the manifolding within the cover plate (12) rather than employ a plurality of tubes for the known and expected result of providing an alternative means recognized in the art to achieve the same result.

With respect to claim 11, the specific width of the channels would have been obvious to one of ordinary skill in the art based merely on the desired number of contact zones desired. It would have been obvious to one of ordinary skill in the art to make the channels narrower so as to provide additional channels on the same sized substrate.

9. Claims 38 and 47 are rejected under 35 U.S.C. 103(a) as being unpatentable over Takayama et al.(Proc. Natl. Acad. Sci.).

The reference of Takayama et al. has been discussed above.

With respect to claim 38, the reference of Takayama et al. discloses that the width of the exposure zone can be between 5 and 100 microns (See page 5546, second column).

Art Unit: 1744

As a result, in the absence of a showing of criticality and/or unexpected results, it would have been obvious to one of ordinary skill in the art to determine the optimum width of the exposure zone based on considerations such as the size of the capillary zone intended to be studied. Whether or not the cells flow in single file would depend on the desired width of the flow channel and/or size of the cells employed in the fluid stream.

With respect to claim 47, while the reference of Takayama et al. discloses that the cells can be immobilized to a target zone prior to an additional step of exposing the immobilized cells to a flow of cells (See Figure 2D and related text), the reference only discloses forming a single distinct exposure zone (See Figure 2D) rather than using a partitioning wall to define a plurality of distinct exposure zones.

However, the use of a cover plate (PDMS) that includes a plurality of channel forming elements would have been obvious such that target region can be simultaneously contacted by a plurality of different flow of cells or cell combinations. Note although the reference of Takayama et al. does not disclose the use of a cover plate with a plurality of distinct flow channels for contacting a target region, it is well established that mere duplication of parts has no patentable significance unless a new and unexpected result is produced (See *In re Harza*, 124 USPQ 378 (CCPA 1960)).

10. Claims 1-53 are rejected under 35 U.S.C. 103(a) as being unpatentable over Takayama et al.(Proc. Natl. Acad. Sci.) in view of Matson et al.(US 5,429,807).

The reference of Takayama et al. discloses a device or system for exposing a substrate surface to one or more fluids that includes a substrate (Petri dish) having a surface containing a

Art Unit: 1744

contiguous target region; a cover plate (PDMS) having a surface capable of fluid-tight contact with the substrate surface; a plurality of fluid-transporting features present in the cover plate surface, the fluid-transporting features separated by at least one partitioning wall; a plurality of fluid inlets (1, 2, 3 in Figure 1B); at least one outlet (See outlet in Figures 1A and 1B). The fluid transporting features that connect the inlets to the “Y” region (See Figures 1A-1D) for distinct exposure zones on the substrate.

While the reference of Takayama et al. discloses maintaining a fluid-tight seal between the cover plate and the substrate surface, the reference is silent as to the use of a “positioning means”.

The reference of Matson et al. discloses that it is known in the art to employ positioning or force applying means (64) to a cover plate (12) and substrate surface (56) so as to maintain the desired fluid-tight seal between a substrate surface and cover plate including fluid-transporting features (14) (See column 5, lines 9-28).

In view of this teaching, it would have been obvious to employ any of the means disclosed by the reference of Matson et al. for positioning the cover plate relative to the substrate surface to maintain a fluid-tight seal for the known and expected result of ensuring that the cover plate maintains a seal relative to the substrate surface during the flow and/or contacting of fluids within the sealed device.

With respect to claim 2, the substrate of Takayama et al. is detachable from the cover plate (See the text on page 5547 corresponding to Fig. 2D).

With respect to claim 3, the substrate is substantially planar (See Figure 1 of Takayama et al.).

Art Unit: 1744

With respect to claims 4-11 and 31-53, while the reference of Takayama et al. only discloses the use of a single “main channel” in the cover plate (PDMS), the use of a plurality of “main channels” provided in the same cover plate would have been obvious to one of ordinary skill in the art for the known and expected result of providing a means for simultaneously forming a plurality of “main channel” target regions on the substrate surface so as to simultaneously perform a plurality of different cell investigations on the same substrate. Note although the reference of Takayama et al. does not disclose the use of a cover plate with a plurality of distinct flow channels for contacting a target region, it is well established that mere duplication of parts has no patentable significance unless a new and unexpected result is produced (See *In re Harza*, 124 USPQ 378 (CCPA 1960)).

With respect to claims 12-28 and 31-53, the reference of Takayama et al. discloses the use of plural types of cells and cell adhesion fluids. As a result, it would have been well within the purview of one having ordinary skill in the art to determine the optimum combination of cells or cell types and other fluids based merely on the specifics of the investigation to be performed.

With respect to claims 29, 30 and 51-53, the reference of Takayama et al. discloses that the cover plate member can be rotated to contact the substrate at a right angle to the original contacting position (See Figure 2D and related text). The reference of Matson et al. also discloses that it is known to reposition the cover plate relative to the substrate surface (See column 6, lines 23-41). As a result, any of the positioning means disclosed by the reference of Matson et al. would be capable of this type of repositioning and its use in the system of the reference of Takayama et al. would be desirable in view of the repositioning discussed by the reference of Takayama et al.

Art Unit: 1744

Conclusion

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to William H. Beisner whose telephone number is 571-272-1269. The examiner can normally be reached on Tues. to Fri. and alt. Mon. from 6:15am to 3:45pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Robert J. Warden can be reached on 571-272-1281. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



William H. Beisner
Primary Examiner
Art Unit 1744

WHB